

CLAIMS

*Sub 13* 1. A heparin-binding protein functionalized by covalently bonding thereto a sugar chain.

2. The heparin-binding protein of claim 1, wherein the sugar chain is selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, an N-linked sugar chain, an O-linked sugar chain and a combination thereof.

*Sub 13* 3. The heparin-binding protein of claim 1 or 2, wherein the heparin-binding protein is a factor belonging to the FGF family or its allied factor.

4. The heparin-binding protein of claim 1, wherein the sugar chain is covalently bonded thereto through a peptide to which the sugar chain can be added.

5. The heparin-binding protein of claim 4, wherein the heparin-binding protein to which the sugar chain is to be covalently bonded is the following (a) or (b):

(a) a protein consisting of the amino acid sequence of SEQ ID NO: 1, 3, 5, 17, 19, 21, 23, 25, 27 or 29;

(b) a protein which consists of the amino acid sequence of SEQ ID NO: 1, 3, 5, 17, 19, 21, 23, 25, 27 or 29 having deletion, substitution, addition or modification of one or several amino acids, which has FGF activity and to which the sugar chain can be added.

6. The heparin-binding protein of claim 1, wherein the sugar chain is bonded to the heparin-binding protein at a site forming a turn in the secondary structure or a site near one of the ends, or a site which will not change the tertiary structure of said protein greatly by addition of the sugar chain.

7. A method for producing a heparin-binding protein functionalized by covalently bonding thereto a sugar chain, comprising the following steps:

- (a) a step in which a cDNA coding for a peptide to which a sugar chain can be added is ligated to a cDNA coding for a heparin-binding protein;
- (b) a step of incorporating the resultant ligated cDNA into an expression vector;
- (c) a step of introducing the expression vector into a host cell having a sugar chain addition pathway; and
- (d) a step of expressing in the host cell a heparin-binding protein to which a sugar chain is covalently bonded through the peptide to which the sugar chain can be added.

8. The method of claim 7, wherein the sugar chain is a sulfated polysaccharide or a glycosaminoglycan, and the peptide to which the sugar chain can be added is a proteoglycan core protein or a part thereof.

9. The method of claim 7, wherein the sugar chain is an N-linked sugar chain, and the peptide to which the sugar chain can be added is a peptide comprising an N-linked sugar chain-added amino acid sequence.

10. The method of claim 7, wherein the sugar chain is an O-linked sugar chain, and the peptide to which the sugar chain can be added is a peptide comprising an O-linked sugar chain-added amino acid sequence.

11. A method for producing a heparin-binding protein functionalized by covalently bonding thereto a sugar chain, comprising a step of allowing the sugar chain to bind to the heparin-binding protein by a chemical binding method.

12. The method of claim 11, wherein the sugar chain is selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, an N-linked sugar chain, an O-linked sugar chain and a combination thereof.

13. The method of any one of claims 7 to 11, wherein the heparin-binding protein is a factor belonging to the FGF family or its allied factor.

14. A pharmaceutical composition containing the heparin-binding protein of any one of claims 1 to 6 as an active ingredient.

15. A method for functionalizing a natural protein having no sugar chain by covalently bonding thereto a sugar chain.